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A microsphere based analytic chemistry system and method for making the same is disclosed in which microspheres or particles carrying bioactive agents may be combined randomly or in ordered fashion and dispersed on a substrate to form an array while maintaining the ability to identify the location of bioactive agents and particles within the array using an optically interrogatable, optical signature encoding scheme. In a preferred embodiment, a modified fiber optic bundle or array is employed as a substrate to produce a high density array. The disclosed system and method have utility for detecting target analytes and screening large libraries of bioactive agents. In a preferred embodiment the methods include detecting a change in an optical property around a microsphere on an array.